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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/471,040	12/23/1999	ULF TILSTAM	SCH-1615-D1	6934
23599 7590 08/17/2007 MILLEN, WHITE, ZELANO & BRANIGAN, P.C. 2200 CLARENDON BLVD. SUITE 1400 ARLINGTON, VA 22201			EXAMINER PESELEV, ELLI	
			ART UNIT 1623	PAPER NUMBER
			MAIL DATE 08/17/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

09/471,040

Applicant(s)

TILSTAM ET AL.

Examiner

Elli Peshev

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 29 June 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 4-15 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 4-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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This application does not contain an abstract of the disclosure as required by 37

CFR 1.72(b). An abstract on a separate sheet is required.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 4-15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2-4 of U.S. Patent No. 6,046,322.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims are directed to crystalline fludarabine-phosphate with a purity of at least 99.5%, while the patented claims are directed to a process for producing said fludarabine-phosphate. A compound is not patentable over the process for its preparation.

Claims 4-15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 7,148,207.

Although the conflicting claims are not identical, they are not patentably distinct from

each other because the present claims are directed to crystalline fludarabine-phosphate with a purity of at least 99.5%, while the patented claims are directed to said compound in a quick-release tablet formulation. A compound is not patentable over the formulation comprising said compound.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 4-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blumbergs et al (U.S. Patent No. 5,110,919) in view of Butler et al (U.S. Patent No. 5,506,352).

Blumbergs et al disclose crystalline fludarabine-phosphate but do not disclose said compound with a purity of at least 99.5%. However, since Butler et al disclose

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purification of a closely analogous arabine-phosphate (column 5, lines 44-67 and column 6, lines 1-18), a person having ordinary skill in the art at the time the claimed invention was made would have been motivated to purify the compound disclosed by Blumbergs et al in accordance with the method disclosed by Butler et al because such a person would have expected to produce a compound having the desired degree of purity.

Applicant's arguments filed June 29, 2007 have been fully considered but they are not persuasive.

Applicant contends that Blumbergs et al warn not to apply processes such as those of Butler et al in an effort to purify fludarabine phosphate by stating that the acidic product is unstable in hot water, that some decomposition occurs during recrystallization and no real improvement in purity results and that with careful handling in the last step, it is possible that the final recrystallization can be avoided. This argument has not been found persuasive since Blumbergs et al also state that "final recrystallization was necessary".

Applicant also contends that the product disclosed by Blumbergs et al is unstable while the product disclosed by Butler et al is stable and that a skilled worker would not use recrystallization process disclosed by Butler et al on fludarabine-phosphate disclosed by Butler et al. Applicant also contends that the product obtained by Butler et al has a degree of purity of only 94.81%. This argument has not been found persuasive. In the declaration by Thomas Wessa and Harald Rabe, it is stated that it is possible to prepare liquid samples of fludarabine phosphate having purity of greater than 99.5%. The

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declaration also states in Experiment 4 that highly pure fludarabine phosphate was placed in a mixture of acetonitrile and water, the samples were dried in a drying cabinet. However, it is not clear from the declaration that the highly pure fludarabine phosphate was actually crystallized. The declaration states that the crystals, which could not be seen visually, were reconstituted in water and their purity was determined. Thus the declaration does not actually shows formation of crystals or the purity of said crystals.

Also, applicant contends that Butler et al disclose recrystallization under acidic conditions under which fludarabine phosphate is unstable. This argument has not been found persuasive since Butler et al also disclose in column 5, lines 36-46, crystallization wherein the aqueous product solution is pumped into the propylene oxide/ethanol solution at a temperature of between 20 C to 25 C and agitating the product until crystallization occurs. It would have been obvious to a person having ordinary skill in the art at the time the claimed invention was made to avoid acidic conditions when crystallizing an unstable product such as fludarabine phosphate.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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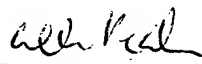
the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elli Peselev whose telephone number is (571) 272-0659. The examiner can normally be reached on 8.00-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Elli Peselev

  
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